UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,320	10/20/2003	Susan A. Kingsman	674523-2030	4549

20999 7590 06/21/2006

FROMMER LAWRENCE & HAUG
745 FIFTH AVENUE- 10TH FL.
NEW YORK, NY 10151

EXAMINER	
LIETO, LOUIS D	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/690,320	KINGSMAN ET AL.	
	Examiner	Art Unit	
	Louis D. Lieto	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-40* is/are pending in the application.

4a) Of the above claim(s) *25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-24 and 26-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/17/02* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/17/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response to the Restriction requirement was received on 4/25/2006. Claims 12-40 are pending in the instant application. Applicant's election with traverse of Group I, claims 19,22,23, drawn to a viral vector system comprising a viral vector pseudotyped with a env nucleotide sequence, which comprises a NOI that is a selection gene, a marker gene, a therapeutic gene, a cDNA library, or a POI, and a VSV-G protein, mutant, homologue or fragment as the species of env protein, is acknowledged.

Claim 25 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/25/2006.

Response to Arguments

Applicant's election with traverse of Group I in the reply filed on 3/29/2006 is acknowledged. Applicant argues that group II and III should be rejoined with group I. However as previously stated: the search of a selection gene, a marker gene, a therapeutic gene, a cDNA library, or a POI and an anti-sense sequence, are quite different from each other. Further, a method of analyzing the function of a gene in a target adipose tissue cell requires a separate search of the art. Thus, the search of groups I-III is not co-extensive. As such, it would be burdensome to search the inventions of groups I-III together.

The requirement is still deemed proper and is therefore made FINAL.

Claims 12-24, 26-30 are under consideration.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 13 and 15 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 13 is drawn to a method of transducing or infecting an adipose cell with a viral vector. The subject matter encompassed by the claim is indistinguishable from that which occurs in nature when a virus infects an adipose cell, such as when CMV infects adipose tissue {Bruggerman et al. (1987) Intervirology 27:32-7; Abstract; pg. 32, col. 1}.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-24, 26-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of transducing a target mammalian adipose tissue cell, with a with viral vector pseudotyped with the VSV-G protein, comprising at least one nucleotide sequence of interest, and said transduced target adipose cell, does not reasonably provide enablement for a method of transducing or infecting an adipose cell with any viral vector to treat any disease associated with adipose tissue metabolism. The specification does not enable

any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims encompass a method of transducing or infecting an adipose cell with any viral vector, which may be a lentiviral vector , such as HIV or EIAV, and wherein said vector is pseudo-typed with at least part of an env protein, such as the VSV-G protein. Wherein the viral vector may comprise a nucleotide of interest. Further the claims are drawn to a method of treating a disease associated with adipose tissue metabolism with a retroviral vector comprising at least one NOI, wherein the viral vector is pseudo-typed with at least part of an env protein, such as the VSV-G protein. Finally the claims also encompass the transduced adipose tissue cell.

The claims are drawn to the transduction or infecting of adipose tissue cells with a vector, such as an HIV vector. However, the specification does not provide any guidance that disclose how to transduce or infect an adipose tissue cell with an HIV vector, *in vivo*, or how to treat an adipose tissue metabolisim disease with an HIV vector *in vivo*. The working examples are solely directed to the transfection of adipose tissue or cells, with an EIAV vector pseudotyped with the VSV-G protein. Munier et al. teaches that adipose tissue cells cannot be infected with HIV-1 *in vivo* {Munier et al. (2003) AIDs 17:2537-2541; Abstract}. Munier teaches that viral entry is the limiting step for adipose cell infection and that the low to non-existent expression of HIV-1 co-receptors is the likely reason why adipose tissue cannot be considered a target tissue for HIV-1 *in vivo* (pg. 2538, col.2 thru pg. 2539, col. 1). Finally, Munier teaches that experiments performed on adipose cells from HIV-1 infected patients strongly suggested that viral DNA remained absent from adipose cells *in vivo* (pg. 2537, col. 1). Given the lack of guidance in the specification on how to transduce adipose cells with HIV, *in vivo*, and the teachings in the art

that said transduction is not possible, the skilled practitioner would be unable to predict how to practice the method in a manner commensurate in scope with the claims, without undue and extensive experimentation.

The claims are drawn to method of treating any disease associated with adipose tissue metabolism. It is noted that the specification does not define what is meant by the phrase adipose tissue metabolism. The phrase reasonably includes diseases such as obesity, diabetes, metabolic syndrome, and anorexia. However, the specification does not provide any guidance on how to use the claimed methods to treat any of these diseases *in vivo*, such as vector dosage, effective methods of administration, or number of times the vector is to be administered. The specification does not disclose any target genes which are the root cause of any disease associated with adipose tissue metabolism. Further, the specification does not provide any guidance on what promoters to use so as to insure the correct expression of the therapeutic NOI so as to treat any disease associated with adipose tissue metabolism.

The claims are drafted to methods of *ex vivo* and *in vivo* gene therapy. However, many unpredictable factors complicate *ex vivo* gene therapy. It is noted that the claims do no limit the administration of the *ex vivo* tranduced adipose cells to subjects of the same species. However, the specification does not provide any guidance on the NOI to be transduced, the number of cells to be administered, the route of administration, the regulatory elements controlling NOI expression or the levels of NOI expression required to treat any adipose tissue metabolism disease. Further, the specification does not provide any guidance on how to over come the immune system mediated hyperacute rejection of xenogeneic tissues or cells due to differences in surface carbohydrate moieties among different species. The hyperacute rejection of

xenotransplants is mediated by circulating antibody response to differences in surface protein carbohydrate modifications and, not MHC expression. Gojo et al. teaches that the T cell response to porcine xenotransplants is secondary to the natural immune barrier of hyperacute rejection of porcine tissues due to the Gal α moiety {Gojo et al. (2000) Transplantation. 69:1995-1999; pgph 12}.

Additionally, with regard to gene therapy, Verma et al. states that in the past, the Achilles heel of gene therapy was gene delivery, and that, most of the approaches suffer from poor efficiency of delivery and transient expression of the gene {Verma et al. (1997) Nature, Vol. 389, page 239, column 3, paragraph 2}. These issues remain as current problems in the field of gene therapy. Pfeifer and Verma state that even "though gene therapy holds great promise for the achievement of this task, the transfer of genetic material into higher organisms still remains an enormous technical challenge { Pfeifer and Verma (2001) Annu. Rev. Genomics. Hum. Genet. 2:177-211; pg. 177, pgph 1}. Johnson-Saliba et al. concurs stating that "although thousands of patients have been involved in clinical trials for gene therapy, using hundreds of different protocols, true success has been limited. A major limitation of gene therapy approaches, especially when non-viral vectors are used, is the poor efficiency of DNA delivery." {Johnson-Saliba et al. (2001) Curr. Drug. Targets 2:371-99; Abstract}. Such problems with delivery continue to plague the field of gene therapy. Shoji et al. has characterized the current state of the art as the "tragic failure of gene therapy" because of poor delivery of gene based-medicines due to the lack of an appropriate vector that "fulfills the necessary requirements, including high transfection efficiency, non-toxicity, non-pathogenicity, non-immunogenicity, [and] non-tumorgenicity." {Shoji et al. (2004) Current Pharmaceutical Design 10 :785-796}. The

specification does not provide sufficient guidance to allow the skilled practitioner to predict how to practice the claimed method in a manner commensurate in scope with the claims, without undue and extensive experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 13,15,18,19,22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Levine et al. {Levine (1998) J. Clin Invest. 101:1557-1564}.

Levine et al. teaches the transfection of adipose cells with an adenovirus NOI comprising the NOI MCSF, which encodes the POI MCSF protein (Abstract, pg. 1557, Methods). Adenoviruses inherently comprise at least a portion of an env protein. Levine et al. teaches that MCSF participates in adipocyte hyperplasia and adipocyte tissue growth. Thus, by teaching all the limitations of the claims as written, Levine et al. anticipates the instant invention as claimed.

Claims 13 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by {Bruggerman et al. (1987) Intervirology 27:32-7}.

Bruggerman et al. provides guidance on the transduction of rat adipose tissue with a CMV virus (Abstract, pg. 32, col. 1-2). Thus, by teaching all the limitations of the claims as written, Bruggerman et al. anticipates the instant invention as claimed.

Claims 12-16, 18, 19, 21-24, 30, 32,33,38,39, are rejected under 35 U.S.C. 102(e) as being anticipated by US 2004/0203017 A1 (10.14.2004) priority to (1.25.2001), hereafter referred to as Dropulic.

Dropulic provides guidance on the transfection of cells with a nucleotide of interest that encodes a product of interest (Abstract). Wherein the nucleotide of interest is comprised within a lentiviral vector pseudotyped with a heterologous viral envelope (env) protein, such as VSV-G (pgph 51). Wherein the cell to be transfected is an adipose cell (pgph 59). Wherein the NOI may encode a marker gene, a therapeutic gene or a sequence from a cDNA library (pgphs 3,10,32-34, 43,45,54,56-58, 73,74,76). Thus, by teaching all the limitations of the claims as written, Dropulic et al. anticipates the instant invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12,13,15-17, 24,30, 31,33,34,39,40 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2004/0203017 A1 (10.14.2004) priority to (1.25.2001), hereafter referred

to as Dropulic, in view of Mitrophanous et al. {Mitrophanous et al. (1999) Gene Therapy 6:1808-1818}

Dropulic provides guidance on the transfection of cells with a nucleotide of interest that encodes a product of interest (Abstract). Wherein the nucleotide of interest is comprised within a lentiviral vector pseudotyped with a heterologous viral envelope (env) protein, such as VSV-G (pgph 51). Wherein the cell to be transfected is an adipose cell (pgph 59). Wherein the NOI may encode a marker gene, a therapeutic gene or a sequence from a cDNA library (pgph 3,10,32-34, 43,45,54,56-58, 73,74,76). Dropulic et al. does not provide guidance on EIAV as the lentiviral vector.

Mitrophanous et al. supplements the guidance of Dropulic by teaching the use of a lentiviral EIAV vector system for gene delivery that has the useful ability of infecting mitotically inactive cells, a trait not-shared by immunodeficiency viruses (Abstract). Further Mitrophanous et al. teaches that EIAV has naturally restricted pathogenicity and a low level of endemic infection indicating that it may be quite useful in many methods of gene therapy (pg.1816, col.1).

Based on the guidance provided by Dropulic on the transfection of adipose cells with a lentiviral vector pseudotyped with VSV-G and encoding an NOI, and the teachings of Mitrophanous et al. on the use of an EIAV vector system for gene delivery, it would be *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of Dropulic by using EIAV as the lentiviral vector pseudotyped with VSV-G and encoding an NOI to transfect the adipose cells.

A practitioner in the art would be motivated to modify the method of Dropulic with the teachings of Mitrophanous et al. in order to transduce mitotically inactive adipose cells, thus

increasing the efficacy of gene delivery.

The person of ordinary skill in the art would have a reasonable expectation of success because the modifying the teachings of Dropulic to use an EIAV as the lentivirus for gene delivery would have been a routine modification in the art at the time of filing.

No claims Allowed.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Dr. Louis D. Lieto
Patent Examiner
Art Unit 1632

Deborah Crouch
DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800 1630